

AMENDMENT

Subject matter to be added is in bold and underlined.

Subject matter to be deleted is in bold and strikethrough.

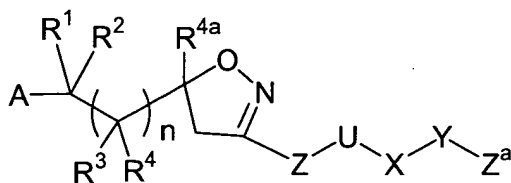
In the Claims:

Please cancel Claims 15-18 without prejudice or disclaimer.

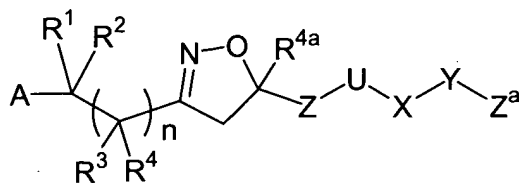
Please enter new claims 19-23 as follows.

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Original) A compound of formula I or II:



I



II

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein;

A is -C(O)NHOH, -C(O)NHO^{R5}, -C(O)NHO^{R6}, -N(OH)CO^{R5}, or -N(OH)CHO;

U is absent or is O, NR^{a1}, C(O), CR^a(OH), C(O)O, OC(O), C(O)NR^{a1}, NR^{a1}C(O), OC(O)O, OC(O)NR^{a1}, NR^{a1}C(O)O, NR^{a1}C(O)NR^{a1}, S(O)_p, S(O)_pNR^{a1}, NR^{a1}S(O)_p, or NR^{a1}SO₂NR^{a1};

X is absent or is C₁₋₁₀ alkylene, C₂₋₁₀ alkenylene, or C₂₋₁₀ alkynylene;

Y is absent or is O, NR^{a1}, S(O)_p, or C(O);

Z is a C₃₋₁₃ carbocycle substituted with 1-5 R^b, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 1-5 R^b;

Z^a is H, C_{3-13} carbocycle substituted with 1-5 R^c , or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 1-5 R^c ;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, $S(O)_p$ -O, O- $S(O)_p$, or $S(O)_p$ - $S(O)_p$ group;

R^1 is Q, C_{1-6} alkylene-Q, C_{2-6} alkenylene-Q, C_{2-6} alkynylene-Q, $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rOC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$, $-(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rOC(O)O(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rOC(O)NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rSO_2NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aSO_2(CR^aR^{a1})_s-Q$, or $-(CR^aR^{a1})_rNR^aSO_2NR^a(CR^aR^{a1})_s-Q$;

Q is, independently at each occurrence, H, CHF_2 , CH_2F , CF_3 , a C_{3-13} carbocycle substituted with 0-5 R^d , or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 0-5 R^d ;

R^2 is Q^1 , C_{1-6} alkylene- Q^1 , C_{2-6} alkenylene- Q^1 , C_{2-6} alkynylene- Q^1 , $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q^1$, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q^1$, $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q^1$, $-(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q^1$, $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$, or $-(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q^1$;

Q^1 is, independently at each occurrence, H, a C_{3-13} carbocycle substituted with 0-5 R^d , or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 0-5 R^d ;

alternatively, R^1 and R^2 combine, along with the carbon atom to which they are attached, to form a 3-7 membered carbocyclic or heterocyclic ring consisting of: carbon

atoms and 0-3 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R³ is Q, C₁₋₆ alkylene-Q, C₂₋₆ alkenylene-Q, C₂₋₆ alkynylene-Q,
-(CR^aR^{al})_rO(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)(CR^aR^{al})_s-Q,
-(CR^aR^{al})_rC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rOC(O)(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)NR^aR^{al},
-(CR^aR^{al})_rC(O)NR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)(CR^aR^{al})_s-Q,
-(CR^aR^{al})_rOC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rOC(O)NR^a(CR^aR^{al})_s-Q,
-(CR^aR^{al})_rNR^aC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)NR^a(CR^aR^{al})_s-Q,
-(CR^aR^{al})_rS(O)_p(CR^aR^{al})_s-Q, -(CR^aR^{al})_rSO₂NR^a(CR^aR^{al})_s-Q,
-(CR^aR^{al})_rNR^aSO₂(CR^aR^{al})_s-Q, or -(CR^aR^{al})_rNR^aSO₂NR^a(CR^aR^{al})_s-Q;

alternatively, R¹ and R³ combine, along with the carbon atom to which they are attached, to form a 3-7 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

alternatively, when R¹ and R³ combine to form a carbocyclic or heterocyclic ring, the R² and R⁴ combine to form a double bond;

R⁴ is Q¹, C₁₋₆ alkylene-Q¹, C₂₋₆ alkenylene-Q¹, C₂₋₆ alkynylene-Q¹,
-(CR^aR^{al})_rO(CR^aR^{al})_s-Q¹, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q¹, -(CR^aR^{al})_rC(O)(CR^aR^{al})_s-Q¹,
-(CR^aR^{al})_rC(O)O(CR^aR^{al})_s-Q¹, -(CR^aR^{al})_rC(O)NR^aR^{al}, or
-(CR^aR^{al})_rC(O)NR^a(CR^aR^{al})_s-Q¹;

alternatively, R³ and R⁴ combine, along with the carbon atom to which they are attached, to form a 3-7 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R^{4a} is Q, C₁₋₆ alkylene-Q, C₂₋₆ alkenylene-Q, C₂₋₆ alkynylene-Q,
-(CR^aR^{al})_rO(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)(CR^aR^{al})_s-Q,
-(CR^aR^{al})_rC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)NR^aR^{al}, -(CR^aR^{al})_rC(O)NR^aOR^a,

$-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})\text{NR}^a(\text{CR}^a\text{R}^{a1})_s\text{-Q}$, $-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{C}(\text{O})(\text{CR}^a\text{R}^{a1})_s\text{-Q}$,
 $-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{C}(\text{O})\text{O}(\text{CR}^a\text{R}^{a1})_s\text{-Q}$, $-(\text{CR}^a\text{R}^{a1})_r\text{S}(\text{O})_p(\text{CR}^a\text{R}^{a1})_s\text{-Q}$, or
 $-(\text{CR}^a\text{R}^{a1})_r\text{SO}_2\text{NR}^a(\text{CR}^a\text{R}^{a1})_s\text{-Q}$;

alternatively, R^1 and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 3-7 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and $\text{S}(\text{O})_p$ and substituted with 0-3 R^d , provided that n is 0;

alternatively, R^3 and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 3-7 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and $\text{S}(\text{O})_p$ and substituted with 0-2 R^d ;

R^a is, independently at each occurrence, H, C_{1-6} alkyl, phenyl, or benzyl;

R^{a1} is, independently at each occurrence, H, C_{1-6} alkyl substituted with 0-1 R^{c1} , C_{2-6} alkenyl substituted with 0-1 R^{c1} , C_{2-6} alkynyl substituted with 0-1 R^{c1} , or $-(\text{CH}_2)_{r-3-8}$ membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N, NR^{a2} , O, and $\text{S}(\text{O})_p$, and substituted with 0-3 R^{c1} ;

alternatively, R^a and R^{a1} when attached to a nitrogen, together with the nitrogen to which they are attached, combine to form a 5 or 6 membered heterocycle consisting of carbon atoms and from 0-1 additional heteroatoms selected from N, NR^{a2} , O, and $\text{S}(\text{O})_p$;

R^{a2} is, independently at each occurrence, C_{1-4} alkyl, phenyl, or benzyl;

R^{a3} is, independently at each occurrence, H, C_{1-6} alkyl substituted with 0-1 R^{c1} , C_{2-6} alkenyl substituted with 0-1 R^{c1} , C_{2-6} alkynyl substituted with 0-1 R^{c1} , or $-(\text{CH}_2)_{r-3-8}$ membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N, NR^{a2} , O, and $\text{S}(\text{O})_p$, and substituted with 0-3 R^{c1} ;

R^b is, independently at each occurrence, H, C_{1-6} alkyl substituted with 0-1 R^{c1} , OR^a , SR^a , Cl, F, Br, I, =O, CN, NO_2 , $-\text{NR}^a\text{R}^{a1}$, $-\text{C}(\text{O})\text{R}^a$, $-\text{C}(\text{O})\text{OR}^a$, $-\text{C}(\text{O})\text{NR}^a\text{R}^{a1}$, $-\text{C}(\text{S})\text{NR}^a\text{R}^{a1}$, $-\text{NR}^a\text{C}(\text{O})\text{NR}^a\text{R}^{a1}$, $-\text{OC}(\text{O})\text{NR}^a\text{R}^{a1}$, $-\text{NR}^a\text{C}(\text{O})\text{OR}^a$, $-\text{S}(\text{O})_2\text{NR}^a\text{R}^{a1}$, $-\text{NR}^a\text{S}(\text{O})_2\text{R}^{a3}$,

$-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{OS}(\text{O})_2\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{S}(\text{O})_{\text{p}}\text{Ra}^3$, CF_3 , CF_2CF_3 , CHF_2 , CH_2F , or phenyl;

R^{c} is, independently at each occurrence, H, OR^{a} , Cl, F, Br, I, $=\text{O}$, CN, NO_2 , CF_3 , CF_2CF_3 , CH_2F , CHF_2 , $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(=\text{NCN})\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(=\text{NR}^{\text{a}})\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(=\text{NOR}^{\text{a}})\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{O})\text{NR}^{\text{a}}\text{OH}$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{O})\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{O})\text{OR}^{\text{a}}$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{S})\text{OR}^{\text{a}}$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{C}(\text{O})\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{S})\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{OC}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{C}(\text{O})\text{OR}^{\text{a}}$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{C}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{S}(\text{O})_{\text{p}}\text{Ra}^3$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{SO}_2\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{SO}_2\text{Ra}^3$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{SO}_2\text{NR}^{\text{a}}\text{Ra}^1$, C_{1-6} alkyl substituted with 0-2 $\text{R}^{\text{c}1}$, C_{2-6} alkenyl substituted with 0-2 $\text{R}^{\text{c}1}$, C_{2-6} alkynyl substituted with 0-2 $\text{R}^{\text{c}1}$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}_{3-10}$ carbocycle substituted with 0-2 $\text{R}^{\text{c}1}$, or $-(\text{CR}^{\text{a}}\text{Ra}^1)_r$ 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $\text{S}(\text{O})_{\text{p}}$, and substituted with 0-2 $\text{R}^{\text{c}1}$;

alternatively, when two R^{c} groups are attached to the same carbon atom, they form a 3-8 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2 $\text{R}^{\text{c}1}$ and consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and $\text{S}(\text{O})_{\text{p}}$, and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when two R^{c} groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or heterocyclic ring D substituted with 0-2 $\text{R}^{\text{c}1}$ and consisting of: carbon atoms and 0-2 heteroatoms selected from N, O, and $\text{S}(\text{O})_{\text{p}}$;

$\text{R}^{\text{c}1}$ is, independently at each occurrence, H, C_{1-4} alkyl, OR^{a} , Cl, F, Br, I, $=\text{O}$, CF_3 , CN, NO_2 , $-\text{C}(\text{O})\text{Ra}^{\text{a}}$, $-\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{Ra}^{\text{a}}$, or $-\text{S}(\text{O})_{\text{p}}\text{Ra}^{\text{a}}$;

R^{d} is, independently at each occurrence, C_{1-6} alkyl, OR^{a} , Cl, F, Br, I, $=\text{O}$, CN, NO_2 , $-\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{C}(\text{O})\text{Ra}^{\text{a}}$, $-\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{OR}^{\text{a}}$, $-\text{C}(\text{S})\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{NR}^{\text{a}}\text{C}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{OC}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{NR}^{\text{a}}\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{S}(\text{O})_2\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{Ra}^3$,

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

-NR^aS(O)₂NR^aR^{a1}, -OS(O)₂NR^aR^{a1}, -S(O)_pR^{a3}, CF₃, CF₂CF₃, C₃₋₁₀ carbocycle, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p;

R⁵ is, independently at each occurrence, C₁₋₁₀ alkyl substituted with 0-2 R^b, or C₁₋₈ alkyl substituted with 0-2 R^e;

R^e is phenyl substituted with 0-2 R^b, or biphenyl substituted with 0-2 R^b;

R⁶ is, phenyl, naphthyl, C₁₋₁₀ alkyl-phenyl-C₁₋₆ alkyl-, C₃₋₁₁ cycloalkyl, C₁₋₆ alkylcarbonyloxy-C₁₋₃ alkyl-, C₁₋₆ alkoxy carbonyloxy-C₁₋₃ alkyl-, C₂₋₁₀ alkoxy carbonyl, C₃₋₆ cycloalkylcarbonyloxy-C₁₋₃ alkyl-, C₃₋₆ cycloalkoxy carbonyloxy-C₁₋₃ alkyl-, C₃₋₆ cycloalkoxy carbonyl, phenoxycarbonyl, phenyloxy carbonyloxy-C₁₋₃ alkyl-, phenylcarbonyloxy-C₁₋₃ alkyl-, C₁₋₆ alkoxy-C₁₋₆ alkylcarbonyloxy-C₁₋₃ alkyl-, [5-(C₁-C₅ alkyl)-1,3-dioxo-cyclopenten-2-one-yl]methyl, [5-(R^a)-1,3-dioxo-cyclopenten-2-one-yl]methyl, (5-aryl-1,3-dioxo-cyclopenten-2-one-yl)methyl, -C₁₋₁₀ alkyl-NR⁷R^{7a}, -CH(R⁸)OC(=O)R⁹, or -CH(R⁸)OC(=O)OR⁹;

R⁷ is H, C₁₋₁₀ alkyl, C₂₋₆ alkenyl, C₃₋₆ cycloalkyl-C₁₋₃ alkyl-, or phenyl-C₁₋₆ alkyl-;

R^{7a} is H, C₁₋₁₀ alkyl, C₂₋₆ alkenyl, C₃₋₆ cycloalkyl-C₁₋₃ alkyl-, or phenyl-C₁₋₆ alkyl-;

R⁸ is H or C₁₋₄ linear alkyl;

R⁹ is H, C₁₋₈ alkyl substituted with 1-2 R^f, C₃₋₈ cycloalkyl substituted with 1-2 R^f, or phenyl substituted with 0-2 R^b;

R^f is, independently at each occurrence, C₁₋₄ alkyl, C₃₋₈ cycloalkyl, C₁₋₅ alkoxy, or phenyl substituted with 0-2 R^b;

n is 0 or 1;

p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, 3, and 4; and

s, at each occurrence, is selected from 0, 1, 2, 3, and 4.

2. (Original) A compound according to Claim 1, wherein:

U is absent or is O, NR^{a1}, C(O), CR^a(OH), C(O)O, OC(O), C(O)NR^{a1}, NR^{a1}C(O), S(O)_p, S(O)_pNR^{a1}, or NR^{a1}S(O)_p;

X is absent or is C₁₋₃ alkylene or C₃₋₄ alkynylene;

Y is absent or is O, NR^{a1}, S(O)_p, or C(O);

Z is a C₅₋₁₀ carbocycle substituted with 1-3 R^b, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 1-3 R^b;

Z^a is H, C₃₋₁₃ carbocycle substituted with 1-3 R^c, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 1-3 R^c;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, S(O)_p-O, O-S(O)_p, or S(O)_p-S(O)_p group;

R¹ is Q, C₁₋₆ alkylene-Q, C₂₋₆ alkenylene-Q, C₂₋₆ alkynylene-Q, -(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rOC(O)(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rOC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rOC(O)NR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rSO₂NR^a(CR^aR^{a1})_s-Q, or -(CR^aR^{a1})_rNR^aSO₂(CR^aR^{a1})_s-Q;

Q is, independently at each occurrence, H, CHF₂, CH₂F, CF₃, a C₃₋₁₃ carbocycle substituted with 0-3 R^d, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-3 R^d;

R² is Q¹, C₁₋₆ alkylene-Q¹, C₂₋₆ alkenylene-Q¹, C₂₋₆ alkynylene-Q¹, -(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q¹, -(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q¹, -(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q¹,

$-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})\text{O}(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}^1$, or $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}^1$;

Q^1 is, independently at each occurrence, H, a C_{3-10} carbocycle substituted with 0-3 R^d , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $\text{S}(\text{O})_p$, and substituted with 0-3 R^d ;

alternatively, R^1 and R^2 , when attached to the same carbon atom, combine to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and $\text{S}(\text{O})_p$ and substituted with 0-2 R^d ;

R^3 is Q, C_{1-6} alkylene-Q, C_{2-6} alkenylene-Q, C_{2-6} alkynylene-Q,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{O}(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})\text{O}(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})\text{NR}^a\text{al}$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{NR}^a\text{C}(\text{O})(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{OC}(\text{O})\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{NR}^a\text{C}(\text{O})\text{O}(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{NR}^a\text{C}(\text{O})\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{S}(\text{O})_p(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{SO}_2\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{NR}^a\text{SO}_2(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$, or $-(\text{CR}^a\text{R}^a\text{al})_r\text{NR}^a\text{SO}_2\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}$;

alternatively, R^1 and R^3 combine, along with the carbon atom to which they are attached, to form a 4-7 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and $\text{S}(\text{O})_p$ and substituted with 0-2 R^d ;

alternatively, when R^1 and R^3 combine to form a carbocyclic or heterocyclic ring, the R^2 and R^4 combine to form a double bond;

R^4 is Q^1 , C_{1-6} alkylene- Q^1 , C_{2-6} alkenylene- Q^1 , C_{2-6} alkynylene- Q^1 ,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{O}(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}^1$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}^1$, $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}^1$,
 $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})\text{O}(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}^1$, or $-(\text{CR}^a\text{R}^a\text{al})_r\text{C}(\text{O})\text{NR}^a(\text{CR}^a\text{R}^a\text{al})_s\text{-Q}^1$;

alternatively, R^3 and R^4 combine, along with the carbon atom to which they are attached, to form a 4-7 membered carbocyclic or heterocyclic ring consisting of: carbon

atoms and 0-3 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R^{4a} is Q, C₁₋₆ alkylene-Q, C₂₋₆ alkenylene-Q, C₂₋₆ alkynylene-Q,
-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q,
-(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rC(O)NR^aOR^a,
-(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q, or
-(CR^aR^{a1})_rSO₂NR^a(CR^aR^{a1})_s-Q;

alternatively, R¹ and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 4-7 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-3 R^d, provided that n is 0;

alternatively, R³ and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 4-7 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-3 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R^a is, independently at each occurrence, H, C₁₋₆ alkyl, phenyl, or benzyl;

R^{a1} is, independently at each occurrence, H, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, or -(CH₂)_r-3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N, NR^{a2}, O, and S(O)_p;

alternatively, R^a and R^{a1} when attached to a nitrogen, together with the nitrogen to which they are attached, combine to form a 5 or 6 membered heterocycle consisting of carbon atoms and from 0-1 additional heteroatoms selected from N, NR^{a2}, O, and S(O)_p;

R^c is, independently at each occurrence, H, OR^a, Cl, F, Br, =O, CN, NO₂, CF₃, CH₂F, CHF₂, CF₂CF₃, -(CR^aR^{a1})_rNR^aR^{a1}, -(CR^aR^{a1})_rC(O)R^{a1}, -(CR^aR^{a1})_rC(O)OR^{a1}, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rNR^aC(O)R^{a1}, -(CR^aR^{a1})_rS(O)_pR^{a3}, -(CR^aR^{a1})_rSO₂NR^aR^{a1}, -(CR^aR^{a1})_rNR^aSO₂R^{a3}, C₁₋₆ alkyl substituted with 0-1 R^{c1},

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

C₂₋₆ alkenyl substituted with 0-1 R^{c1}, C₂₋₆ alkynyl substituted with 0-1 R^{c1}, -(CH₂)_r-C₃₋₆ carbocycle substituted with 0-2 R^{c1}, or -(CH₂)_r-5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-2 R^{c1};

alternatively, when two R^c groups are attached to the same carbon atom, they form a 3-8 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2 R^{c1} and consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and S(O)_p, and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when two R^c groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or heterocyclic ring D substituted with 0-2 R^{c1} and consisting of: carbon atoms and 0-2 heteroatoms selected from N, O, and S(O)_p;

R^d is, independently at each occurrence, C₁₋₆ alkyl, OR^a, Cl, F, Br, =O, CN, NO₂, -NR^aR^{a1}, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^{a1}, -S(O)₂NR^aR^{a1}, -NR^aS(O)₂R^{a3}, -S(O)_pR^{a3}, CF₃, C₃₋₆ carbocycle, or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p;

R⁵ is, independently at each occurrence, C₁₋₆ alkyl substituted with 0-2 R^b, or C₁₋₄ alkyl substituted with 0-2 R^e; and

R^f is, independently at each occurrence, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₁₋₅ alkoxy, or phenyl substituted with 0-2 R^b.

3. (Original) A compound according to Claim 2, wherein:

A is -C(O)NHOH or -N(OH)CHO;

U is absent or is O, NR^{a1}, C(O), CR^a(OH), C(O)NR^{a1}, NR^{a1}C(O), S(O)_p, S(O)_pNR^{a1}, or NR^{a1}S(O)_p;

X is absent or is methylene, ethylene, propynylene, or butynylene;

Z is a C₅₋₁₀ carbocycle substituted with 1-2 R^b, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 1-2 R^b;

Z^a is H, C₅₋₁₀ carbocycle substituted with 1-3 R^c, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 1-3 R^c;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, S(O)_p-O, O-S(O)_p, or S(O)_p-S(O)_p group;

R¹ is Q, C₁₋₆ alkylene-Q, C₂₋₆ alkenylene-Q, C₂₋₆ alkynylene-Q, -(CR^aR^{al})_rO(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)NR^aR^{al}, -(CR^aR^{al})_rC(O)NR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)(CR^aR^{al})_s-Q, -(CR^aR^{al})_rOC(O)NR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rS(O)_p(CR^aR^{al})_s-Q, -(CR^aR^{al})_rSO₂NR^a(CR^aR^{al})_s-Q, or -(CR^aR^{al})_rNR^aSO₂(CR^aR^{al})_s-Q;

Q is, independently at each occurrence, H, a C₃₋₈ carbocycle substituted with 0-3 R^d, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-3 R^d;

R² is Q¹, C₁₋₆ alkylene-Q¹, C₂₋₆ alkenylene-Q¹, -CR^aR^{al})_rO(CR^aR^{al})_s-Q¹, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q¹, or -(CR^aR^{al})_rC(O)(CR^aR^{al})_s-Q¹;

Q¹ is, independently at each occurrence, H, a C₅₋₁₀ carbocycle substituted with 0-2 R^d, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-2 R^d;

R³ is Q, C₁₋₆ alkylene-Q, C₂₋₆ alkenylene-Q, C₂₋₆ alkynylene-Q, -(CR^aR^{al})_rO(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)NR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rS(O)_p(CR^aR^{al})_s-Q,

$-(\text{CR}^a\text{Ra}^1)_r\text{SO}_2\text{NR}^a(\text{CR}^a\text{Ra}^1)_s-\text{Q}$, or $-(\text{CR}^a\text{Ra}^1)_r\text{NR}^a\text{SO}_2(\text{CR}^a\text{Ra}^1)_s-\text{Q}$;

R^4 is Q^1 , C_{1-6} alkylene- Q^1 , C_{2-6} alkenylene- Q^1 , $-(\text{CR}^a\text{Ra}^1)_r\text{O}(\text{CR}^a\text{Ra}^1)_s-\text{Q}^1$,
 $-(\text{CR}^a\text{Ra}^1)_r\text{NR}^a(\text{CR}^a\text{Ra}^1)_s-\text{Q}^1$, or $-(\text{CR}^a\text{Ra}^1)_r\text{C}(\text{O})(\text{CR}^a\text{Ra}^1)_s-\text{Q}^1$;

R^{4a} is Q , C_{1-4} alkylene- Q , $-(\text{CH}_2)_r\text{O}(\text{CH}_2)_s-\text{Q}$, $-(\text{CH}_2)_r\text{NR}^a(\text{CH}_2)_s-\text{Q}$,
 $-(\text{CH}_2)_r\text{C}(\text{O})(\text{CH}_2)_s-\text{Q}$, $-(\text{CH}_2)_r\text{C}(\text{O})\text{O}(\text{CH}_2)_s-\text{Q}$, $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a\text{Ra}^1$,
 $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a\text{OR}^a$, $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a(\text{CH}_2)_s-\text{Q}$, $-(\text{CH}_2)_r\text{NR}^a\text{C}(\text{O})(\text{CH}_2)_s-\text{Q}$, or
 $-(\text{CH}_2)_r\text{NR}^a\text{C}(\text{O})\text{O}(\text{CH}_2)_s-\text{Q}$;

R^{a3} is, independently at each occurrence, H , C_{1-6} alkyl, C_{2-6} alkenyl, or $-(\text{CH}_2)_{r-3-8}$
membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring
heteroatoms selected from N , NR^{a2} , O , and $\text{S}(\text{O})_p$, and substituted with 0-3 R^{c1} ;

R^c is, independently at each occurrence, H , OR^a , Cl , F , Br , $=\text{O}$, CF_3 , CH_2F , CHF_2 ,
 $-(\text{CR}^a\text{Ra}^1)_r\text{NR}^a\text{Ra}^1$, $-(\text{CR}^a\text{Ra}^1)_r\text{C}(\text{O})\text{Ra}^1$, $-(\text{CR}^a\text{Ra}^1)_r\text{C}(\text{O})\text{OR}^a$, $-(\text{CR}^a\text{Ra}^1)_r\text{C}(\text{O})\text{NR}^a\text{Ra}^1$,
 $-(\text{CR}^a\text{Ra}^1)_r\text{NR}^a\text{C}(\text{O})\text{Ra}^1$, $-(\text{CR}^a\text{Ra}^1)_r\text{S}(\text{O})_p\text{Ra}^3$, $-(\text{CR}^a\text{Ra}^1)_r\text{SO}_2\text{NR}^a\text{Ra}^1$,
 $-(\text{CR}^a\text{Ra}^1)_r\text{NR}^a\text{SO}_2\text{Ra}^3$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl substituted
with 0-1 R^{c1} , phenyl substituted with 0-2 R^{c1} , or 5-6 membered heterocycle consisting of
carbon atoms and 1-4 heteroatoms selected from N , O , and $\text{S}(\text{O})_p$, and substituted with 0-2
 R^{c1} ;

alternatively, when two R^c groups are attached to adjacent carbon atoms, together
with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or
heterocyclic ring D substituted with 0-2 R^{c1} and consisting of: carbon atoms and 0-2
heteroatoms selected from N , O , and $\text{S}(\text{O})_p$;

R^d is, independently at each occurrence, C_{1-6} alkyl, OR^a , Cl , F , Br , $=\text{O}$, $-\text{NR}^a\text{Ra}^1$,
 $-\text{C}(\text{O})\text{Ra}^1$, $-\text{C}(\text{O})\text{OR}^a$, $-\text{C}(\text{O})\text{NR}^a\text{Ra}^1$, $-\text{S}(\text{O})_2\text{NR}^a\text{Ra}^1$, $-\text{NR}^a\text{S}(\text{O})_2\text{Ra}^3$, $-\text{S}(\text{O})_p\text{Ra}^3$, CF_3 , or
phenyl;

R^5 is, independently at each occurrence, C_{1-4} alkyl substituted with 0-2 R^b , or
 C_{1-4} alkyl substituted with 0-2 R^e ;

r, at each occurrence, is selected from 0, 1, 2, and 3; and
s, at each occurrence, is selected from 0, 1, 2, and 3.

4. (Original) A compound according to Claim 3, wherein:

A is -C(O)NHOH;

Z is phenyl substituted with 1-2 R^b, naphthyl substituted with 1-2 R^b, or pyridyl substituted with 1-2 R^b;

Z^a is phenyl substituted with 1-3 R^c, naphthyl substituted with 1-3 R^c, or a heterocycle substituted with 1-3 R^c and selected from furanyl, tetrahydrofuranyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isoxazolyl, 4,5-dihydro-isoxazolyl, thienyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyrimidinyl, piperazinyl, piperidinyl, pyranyl, pyrazinyl, pyrazolyl, pyridoimidazolyl, pyrrolidinyl, pyrrolyl, indolyl, indolinyl, benzimidazolyl, benzothiazinyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benzisoxazolyl, benzisothiazolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydro-isoquinolinyl, indazolyl, isobenzofuranyl, isoindazolyl, isoindolinyl, isoindolyl, methylenedioxyphenyl, quinazolinyl, 1,1-dioxido-2,3-dihydro-4H-1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2H-1-benzothiopyran-4-yl, 3,4-dihydro-2H-chomen-4-yl, 2H-chomen-4-yl, and pyrazolo[1,5-a]pyridinyl;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, S(O)_p-O, O-S(O)_p, or S(O)_p-S(O)_p group;

R¹ is selected from Q, C₁₋₆ alkylene-Q, -(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q, or -(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q;

Q is, independently at each occurrence, H, a C₃₋₆ carbocycle substituted with 0-3 R^d, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-3 R^d;

R² is Q¹ or C₁₋₆ alkylene-Q¹;

Q^1 is, independently at each occurrence, H, phenyl substituted with 0-2 R^d , or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 0-2 R^d ;

R^3 is Q, C_{1-4} alkylene-Q, C_{2-4} alkenylene-Q, C_{2-4} alkynylene-Q, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rSO_2NR^a(CR^aR^{a1})_s-Q$, or $-(CR^aR^{a1})_rNR^aSO_2(CR^aR^{a1})_s-Q$;

R^4 is Q^1 or C_{1-6} alkylene- Q^1 ;

R^{4a} is Q, $-CH_2-Q$, $-CH_2O(CH_2)_s-Q$, $-CH_2NR^a(CH_2)_s-Q$, $-CH_2C(O)(CH_2)_s-Q$, $-CH_2C(O)O(CH_2)_s-Q$, $-CH_2C(O)NR^aR^{a1}$, $-(CH_2)_rC(O)NR^aOR^a$, $-CH_2C(O)NR^a(CH_2)_s-Q$, $-CH_2NR^aC(O)(CH_2)_s-Q$, or $-CH_2NR^aC(O)O(CH_2)_s-Q$;

R^{a1} is, independently at each occurrence, H, C_{1-6} alkyl, phenyl, or benzyl;

R^{a3} is, independently at each occurrence, H, C_{1-6} alkyl, phenyl, or benzyl;

R^c is, independently at each occurrence, H, OR^a , Cl, F, Br, =O, CF_3 , CH_2F , CHF_2 , $-(CR^aR^{a1})_rNR^aR^{a1}$, $-(CR^aR^{a1})_rC(O)R^{a1}$, $-(CR^aR^{a1})_rC(O)OR^{a1}$, $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$, $-(CR^aR^{a1})_rNR^aC(O)R^{a1}$, $-(CR^aR^{a1})_rS(O)_pR^{a3}$, $-(CR^aR^{a1})_rSO_2NR^aR^{a1}$, $-(CR^aR^{a1})_rNR^aSO_2R^{a3}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl substituted with 0-2 R^{c1} , or 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 0-2 R^{c1} ; and

alternatively, when two R^c groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-6 membered carbocyclic or heterocyclic ring D substituted with 0-2 R^{c1} and consisting of: carbon atoms and 0-2 heteroatoms selected from N, O, and $S(O)_p$.

5. (Original) A compound according to Claim 4, wherein:

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

U is absent or is O, NR^{a1}, C(O), CR^a(OH), C(O)NR^{a1}, or NR^{a1}C(O);

X is absent or is methylene or butynylene;

Y is absent or is O;

Z is phenyl substituted with 1-2 R^b;

Z^a is naphthyl substituted with 1-3 R^c, or a heterocycle substituted with 1-3 R^c and selected from furanyl, tetrahydrofuranyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isoxazolyl, 4,5-dihydro-isoxazolyl, thienyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyrimidinyl, pyranyl, pyrazinyl, pyrazolyl, pyridoimidazolyl, pyrrolidinyl, pyrrolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydro-isoquinolinyl, imidazolyl, benzimidazolyl, benzothiazinyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benzisoxazolyl, benzisothiazolyl, indolyl, indolinyl, indazolyl, isobenzofuranyl, isoindazolyl, isoindolinyl, isoindolyl, quinazolinyl, 1,1-dioxido-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2*H*-1-benzothiopyran-4-yl, 3,4-dihydro-2*H*-chomen-4-yl, 2*H*-chomen-4-yl, and pyrazolo[1,5-*a*]pyridinyl;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, S(O)_p-O, O-S(O)_p, or S(O)_p-S(O)_p group;

R¹ is Q, C₁₋₆ alkylene-Q, -(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q, or -(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q;

Q is, independently at each occurrence, H, a C₃₋₆ carbocycle substituted with 0-3 R^d, or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-3 R^d;

R² is H or C₁₋₆ alkylene-Q¹;

R³ is Q, C₁₋₄ alkylene-Q, C₂₋₄ alkenylene-Q, C₂₋₄ alkynylene-Q, -(CH₂)_rNR^a(CH₂)_s-Q, -(CH₂)_rNR^aC(O)(CH₂)_s-Q, -(CH₂)_rNR^aC(O)O(CR^aR^{a1})_s-Q, -(CH₂)_rNR^aC(O)NR^a(CH₂)_s-Q, -(CH₂)_rS(O)_p(CH₂)_s-Q, or -(CH₂)_rNR^aSO₂(CH₂)_s-Q;

R⁴ is H or C₁₋₆ alkylene-Q¹;

R^{4a} is Q, $-\text{CH}_2\text{-Q}$, $-\text{CH}_2\text{O-Q}$, $-\text{CH}_2\text{NR}^a\text{-Q}$, $-\text{CH}_2\text{C(O)}_s\text{-Q}$, $-\text{CH}_2\text{C(O)O-Q}$,
 $-\text{CH}_2\text{C(O)NR}^a\text{Ra}^1$, $-\text{C(O)NR}^a\text{OR}^a$, $-\text{CH}_2\text{C(O)NR}^a\text{-Q}$, or $-\text{CH}_2\text{NR}^a\text{C(O)O-Q}$;

R^a is, independently at each occurrence, H, or C_{1-4} alkyl;

Ra^1 is, independently at each occurrence, H, or C_{1-4} alkyl;

Ra^3 is, independently at each occurrence, H, C_{1-4} alkyl, phenyl, or benzyl;

R^c is, independently at each occurrence, C_{1-6} alkyl, C_{2-6} alkenyl,
 C_{2-6} alkynyl, OR^a , Cl, F, Br, $=\text{O}$, CF_3 , CH_2F , CHF_2 , $-\text{NR}^a\text{Ra}^1$, $-(\text{CR}^a\text{Ra}^1)_r\text{C(O)Ra}^1$,
 $-(\text{CR}^a\text{Ra}^1)_r\text{C(O)OR}^a$, $-(\text{CR}^a\text{Ra}^1)_r\text{C(O)NR}^a\text{Ra}^1$, $-(\text{CR}^a\text{Ra}^1)_r\text{NR}^a\text{C(O)Ra}^1$,
 $-(\text{CR}^a\text{Ra}^1)_r\text{S(O)}_p\text{Ra}^3$, $-(\text{CR}^a\text{Ra}^1)_r\text{SO}_2\text{NR}^a\text{Ra}^1$, $-(\text{CR}^a\text{Ra}^1)_r\text{NR}^a\text{SO}_2\text{Ra}^3$, or phenyl; and

alternatively, when two R^c groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-6 membered carbocyclic or heterocyclic ring D substituted with 0-1 R^{c1} and consisting of: carbon atoms and 0-2 heteroatoms selected from N, O, and S(O)_p .

6. (Original) A compound according to Claim 5, wherein:

U is absent or is O, NR^a , C(O) , or $\text{CR}^a(\text{OH})$;

Y is absent;

R^1 is H, C_{1-4} alkylene-Q, $-(\text{CH}_2)_r\text{NR}^a(\text{CH}_2)_s\text{-Q}$, or
 $-(\text{CH}_2)_r\text{NR}^a\text{C(O)O(CR}^a\text{Ra}^1)_s\text{-Q}$;

R^2 is H, CH_3 , CH_2CH_3 , $\text{CH}_2\text{CH}_2\text{CH}_3$, or $\text{CH}(\text{CH}_3)_2$;

R^3 is Q, C_{1-4} alkylene-Q, $-(\text{CH}_2)_r\text{NR}^a(\text{CH}_2)_s\text{-Q}$, $-(\text{CH}_2)_r\text{NR}^a\text{C(O)(CH}_2)_s\text{-Q}$,
 $-(\text{CH}_2)_r\text{NR}^a\text{C(O)O(CR}^a\text{Ra}^1)_s\text{-Q}$, $-(\text{CH}_2)_r\text{NR}^a\text{C(O)NR}^a(\text{CH}_2)_s\text{-Q}$, $-(\text{CH}_2)_r\text{S(CH}_2)_s\text{-Q}$, or
 $-(\text{CH}_2)_r\text{NR}^a\text{SO}_2(\text{CH}_2)_s\text{-Q}$;

R^4 is H, CH_3 , CH_2CH_3 , $\text{CH}_2\text{CH}_2\text{CH}_3$, or $\text{CH}(\text{CH}_3)_2$;

R^{4a} is Q, $-\text{CH}_2\text{-Q}$, $-\text{CH}_2\text{O-Q}$, $-\text{CH}_2\text{NR}^a\text{-Q}$, $-\text{CH}_2\text{C(O)}_s\text{-Q}$, $-\text{CH}_2\text{C(O)O-Q}$,
 $-\text{CH}_2\text{C(O)NR}^a\text{Ra}^1$, $-\text{C(O)NR}^a\text{OR}^a$, or $-\text{CH}_2\text{C(O)NR}^a\text{-Q}$;

r, at each occurrence, is selected from 0, 1, and 2; and

s, at each occurrence, is selected from 0, 1, and 2.

7. (Original) A compound according to Claim 6, wherein:

U is O, NR^{a1} , or $\text{CR}^{\text{a}}(\text{OH})$;

Z^{a} is naphthyl substituted with 1-3 R^{c} , or a heterocycle substituted with 1-3 R^{c} and selected from pyridyl, quinoliny, imidazolyl, benzimidazolyl, indolyl, 1,1-dioxido-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2*H*-1-benzothiopyran-4-yl, 3,4-dihydro-2*H*-chomen-4-yl, 2*H*-chomen-4-yl, pyrazolyl, and pyrazolo[1,5-*a*]pyridinyl;

R^1 is H, CH_3 , CH_2CH_3 , $\text{CH}_2\text{CH}_2\text{CH}_3$, $\text{CH}(\text{CH}_3)_2$, NH_2 , or $-\text{NHC}(\text{O})\text{OC}(\text{CH}_3)_3$;

R^2 is H or CH_3 ;

R^3 is Q, C_{1-4} alkylene-Q, $-\text{NR}^{\text{a}}(\text{CH}_2)_s\text{-Q}$, $-\text{NR}^{\text{a}}\text{C}(\text{O})(\text{CH}_2)_s\text{-Q}$, $-\text{NR}^{\text{a}}\text{C}(\text{O})\text{O}(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_s\text{-Q}$, $-\text{NR}^{\text{a}}\text{C}(\text{O})\text{NR}^{\text{a}}(\text{CH}_2)_s\text{-Q}$, $-\text{S}(\text{CH}_2)_s\text{-Q}$, or $-\text{NR}^{\text{a}}\text{SO}_2(\text{CH}_2)_s\text{-Q}$;

$\text{R}^{4\text{a}}$ is Q, $-\text{CH}_2\text{-Q}$, $-\text{CH}_2\text{O-Q}$, $-\text{CH}_2\text{NR}^{\text{a}}\text{-Q}$, or $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{OR}^{\text{a}}$;

Q is, independently at each occurrence, H, phenyl substituted with 0-3 R^{d} , or a 5-6 membered heterocycle consisting of carbon atoms and 1-2 heteroatoms selected from N, O, and $\text{S}(\text{O})_p$, and substituted with 0-3 R^{d} ;

R^{b} is, independently at each occurrence, H, C_{1-6} alkyl, OR^{a} , Cl, F, Br, $-\text{NR}^{\text{a}}\text{R}^{\text{a1}}$, $-\text{C}(\text{O})\text{R}^{\text{a}}$, $-\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a1}}$, $-\text{S}(\text{O})_2\text{NR}^{\text{a}}\text{R}^{\text{a1}}$, $-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{R}^{\text{a3}}$, $-\text{S}(\text{O})_p\text{R}^{\text{a3}}$, or CF_3 ;

R^{c} is, independently at each occurrence, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, OR^{a} , Cl, F, Br, $=\text{O}$, CF_3 , $-\text{NR}^{\text{a}}\text{R}^{\text{a1}}$, $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{C}(\text{O})\text{R}^{\text{a1}}$, $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{C}(\text{O})\text{OR}^{\text{a1}}$, $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a1}}$, $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{NR}^{\text{a}}\text{C}(\text{O})\text{R}^{\text{a1}}$, $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{S}(\text{O})_p\text{R}^{\text{a3}}$, $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{SO}_2\text{NR}^{\text{a}}\text{R}^{\text{a1}}$, or $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{NR}^{\text{a}}\text{SO}_2\text{R}^{\text{a3}}$; and

alternatively, when two R^{c} groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-6 membered saturated ring consisting of: carbon atoms and 0-1 heteroatoms selected from N, O, and $\text{S}(\text{O})_p$.

8. (Original) A compound according to Claim 1, wherein the compound is selected from the group:

N-hydroxy-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-acetamide;

N-hydroxy-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

N-hydroxy-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-5-morpholin-4-ylmethyl-4,5-dihydro-isoxazol-5-yl}-acetamide;

N-hydroxy-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-5-piperazin-1-ylmethyl-4,5-dihydro-isoxazol-5-yl}-acetamide;

2-{5-dimethylaminomethyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-N-hydroxy-acetamide;

N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

N-hydroxy-3-methyl-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-butyramide;

(1-hydroxycarbamoyl-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-ethyl)-carbamic acid tert-butyl ester;

2-amino-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

3-amino-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-3-methylsulfanyl-propionamide;

N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-3-morpholin-4-yl-propionamide;

3-amino-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-butyramide;

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

furan-2-carboxylic acid (2-hydroxycarbamoyl-1-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-ethyl)-amide;

N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-3-pyrrolidin-1-yl-propionamide;

3-acetyl-amino-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

3-dimethyl-amino-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

3-(3-ethyl-ureido)-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

N-hydroxy-3-methanesulfonylamino-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

3-[(furan-2-ylmethyl)-amino]-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

3-benzyl-amino-N-hydroxy-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

(2-hydroxycarbamoyl-1-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-ethyl)-carbamic acid isobutyl ester;

N-hydroxy-3-{5-methyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

N-hydroxy-3-{5-hydroxymethyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-propionamide;

5-(2-hydroxycarbamoyl-ethyl)-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazole-5-carboxylic acid methyl ester;

5-(2-hydroxycarbamoyl-ethyl)-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazole-5-carboxylic acid hydroxyamide;

2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-cyclopent-1-enecarboxylic acid hydroxyamide;

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

cis-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-cyclopentanecarboxylic acid hydroxyamide;

cis-4-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-pyrrolidine-3-carboxylic acid hydroxyamide;

cis-4-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-tetrahydro-furan-3-carboxylic acid hydroxyamide;

N-hydroxy-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-1-oxa-2-aza-spiro[4.5]dec-2-en-6-yl}-acetamide;

N-hydroxy-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-1,8-dioxo-2-aza-spiro[4.5]dec-2-en-6-yl}-acetamide;

6-hydroxycarbamoylmethyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-1-oxa-2,8-diaza-spiro[4.5]dec-2-ene-8-carboxylic acid tert-butyl ester;

N-hydroxy-2-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-1-oxa-2,8-diaza-spiro[4.5]dec-2-en-6-yl}-acetamide;

N-hydroxy-2-{8-methyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-1-oxa-2,8-diaza-spiro[4.5]dec-2-en-6-yl}-acetamide;

2-{8-acetyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-1-oxa-2,8-diaza-spiro[4.5]dec-2-en-6-yl}-N-hydroxy-acetamide;

7-methyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-6-oxo-1-oxa-2,7-diaza-spiro[4.4]non-2-ene-9-carboxylic acid hydroxyamide;

7-methyl-3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-6-oxo-1-oxa-2,7-diaza-spiro[4.5]dec-2-ene-10-carboxylic acid hydroxyamide;

N-hydroxy-2-(4-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-tetrahydro-pyran-4-yl)-acetamide;

2-(1-acetyl-4-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-piperidin-4-yl)-N-hydroxy-acetamide;

3-hydroxycarbamoylmethyl-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-pyrrolidine-1-carboxylic acid tert-butyl ester;

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

N-hydroxy-2-(3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-pyrrolidin-3-yl)-acetamide; and

N-hydroxy-2-(1-methyl-3-{3-[4-(2-methyl-quinolin-4-ylmethoxy)-phenyl]-4,5-dihydro-isoxazol-5-yl}-pyrrolidin-3-yl)-acetamide;
or a stereoisomer or pharmaceutically acceptable salt form thereof.

9. (Original) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt form thereof.

10. (Withdrawn) A method for treating an inflammatory disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt form thereof.

11. (Withdrawn) A method of treating a condition or disease mediated by MMPs, TACE, aggrecanase, or a combination thereof in a mammal, comprising: administering to the mammal in need of such treatment a therapeutically effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt form thereof.

12. (Withdrawn) A method comprising: administering a compound according to Claim 1 or a pharmaceutically acceptable salt form thereof, in an amount effective to treat a condition or disease mediated by MMPs, TACE, aggrecanase, or a combination thereof.

13. (Withdrawn) A method of treating according to Claim 12, wherein the disease or condition is selected from to as acute infection, acute phase response, age related macular degeneration, alcoholic liver disease, allergy, allergic asthma, anorexia, aneurism, aortic aneurism, asthma, atherosclerosis, atopic dermatitis, autoimmune disease, autoimmune hepatitis, Bechet's disease, cachexia, calcium pyrophosphate dihydrate deposition disease, cardiovascular effects, chronic fatigue syndrome, chronic obstruction pulmonary disease, coagulation, congestive heart failure, corneal ulceration, Crohn's disease,

enteropathic arthropathy, Felty's syndrome, fever, fibromyalgia syndrome, fibrotic disease, gingivitis, glucocorticoid withdrawal syndrome, gout, graft versus host disease, hemorrhage, HIV infection, hyperoxic alveolar injury, infectious arthritis, inflammation, intermittent hydrarthrosis, Lyme disease, meningitis, multiple sclerosis, myasthenia gravis, mycobacterial infection, neovascular glaucoma, osteoarthritis, pelvic inflammatory disease, periodontitis, polymyositis/dermatomyositis, post-ischaemic reperfusion injury, post-radiation asthenia, psoriasis, psoriatic arthritis, pulmonary emphysema, pyoderma gangrenosum, relapsing polychondritis, Reiter's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, sepsis syndrome, Still's disease, shock, Sjogren's syndrome, skin inflammatory diseases, solid tumor growth and tumor invasion by secondary metastases, spondylitis, stroke, systemic lupus erythematosus, ulcerative colitis, uveitis, vasculitis, and Wegener's granulomatosis.

14. (Withdrawn) A method for treating inflammatory disorders, comprising:
administering, to a host in need of such treatment, a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt form thereof, in combination with one or more additional anti-inflammatory agents selected from selective COX-2 inhibitors, interleukin-1 antagonists, dihydroorotate synthase inhibitors, p38 MAP kinase inhibitors, TNF- α inhibitors and TNF- α antibody or protein sequestration agents.

15-18. (Canceled)

19. (New) A compound according to Claim 2, wherein:

A is -C(O)NHOH or -N(OH)CHO;

U is absent or is O, NR^{a1}, C(O), CR^a(OH), C(O)NR^{a1}, NR^{a1}C(O), S(O)_p, S(O)_pNR^{a1}, or NR^{a1}S(O)_p;

X is absent or is methylene, ethylene, propynylene, or butynylene;

Z is a C₅₋₁₀ carbocycle substituted with 1-2 R^b, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 1-2 R^b;

Z^a is H, C_{5-10} carbocycle substituted with 1-3 R^c , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 1-3 R^c ;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, $S(O)_p$ -O, O- $S(O)_p$, or $S(O)_p$ - $S(O)_p$ group;

R^1 is Q, C_{1-6} alkylene-Q, C_{2-6} alkenylene-Q, C_{2-6} alkynylene-Q, $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$, $-(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rOC(O)NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rSO_2NR^a(CR^aR^{a1})_s-Q$, or $-(CR^aR^{a1})_rNR^aSO_2(CR^aR^{a1})_s-Q$;

Q is, independently at each occurrence, H, a C_{3-8} carbocycle substituted with 0-3 R^d , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 0-3 R^d ;

R^2 is Q^1 , C_{1-6} alkylene- Q^1 , C_{2-6} alkenylene- Q^1 , $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q^1$, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q^1$, or $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q^1$;

Q^1 is, independently at each occurrence, H, a C_{5-10} carbocycle substituted with 0-2 R^d , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 0-2 R^d ;

R^3 is Q, C_{1-6} alkylene-Q, C_{2-6} alkenylene-Q, C_{2-6} alkynylene-Q, $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rNR^aC(O)NR^a(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q$, $-(CR^aR^{a1})_rSO_2NR^a(CR^aR^{a1})_s-Q$, or $-(CR^aR^{a1})_rNR^aSO_2(CR^aR^{a1})_s-Q$;

alternatively, R^1 and R^3 combine, along with the carbon atom to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ and substituted with 0-2 R^d ;

alternatively, when R^1 and R^3 combine to form a carbocyclic or heterocyclic ring, the R^2 and R^4 combine to form a double bond;

R^4 is Q^1 , C_{1-6} alkylene- Q^1 , C_{2-6} alkenylene- Q^1 , $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q^1$, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q^1$, or $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q^1$;

alternatively, R^3 and R^4 combine, along with the carbon atom to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ and substituted with 0-2 R^d ;

R^{4a} is Q, C_{1-4} alkylene-Q, $-(CH_2)_rO(CH_2)_s-Q$, $-(CH_2)_rNR^a(CH_2)_s-Q$, $-(CH_2)_rC(O)(CH_2)_s-Q$, $-(CH_2)_rC(O)O(CH_2)_s-Q$, $-(CH_2)_rC(O)NR^aR^{a1}$, $-(CH_2)_rC(O)NR^aOR^a$, $-(CH_2)_rC(O)NR^a(CH_2)_s-Q$, $-(CH_2)_rNR^aC(O)(CH_2)_s-Q$, or $-(CH_2)_rNR^aC(O)O(CH_2)_s-Q$;

alternatively, R^1 and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ and substituted with 0-3 R^d , provided that n is 0;

alternatively, R^3 and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ and substituted with 0-2 R^d ;

R^a is, independently at each occurrence, H, C_{1-6} alkyl, C_{2-6} alkenyl, or $-(CH_2)_{r-3-8}$ membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N, NR^{a2} , O, and $S(O)_p$, and substituted with 0-3 R^{c1} ;

R^c is, independently at each occurrence, H, OR^a , Cl, F, Br, =O, CF_3 , CH_2F , CHF_2 ,

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

$-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{O})\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{O})\text{OR}^{\text{a}1}$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{C}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$,
 $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{C}(\text{O})\text{Ra}^1$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{S}(\text{O})_p\text{Ra}^3$, $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{SO}_2\text{NR}^{\text{a}}\text{Ra}^1$,
 $-(\text{CR}^{\text{a}}\text{Ra}^1)_r\text{NR}^{\text{a}}\text{SO}_2\text{Ra}^3$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl substituted with 0-1 $\text{R}^{\text{c}1}$, phenyl substituted with 0-2 $\text{R}^{\text{c}1}$, or 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $\text{S}(\text{O})_p$, and substituted with 0-2 $\text{R}^{\text{c}1}$;

alternatively, when two R^{c} groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or heterocyclic ring D substituted with 0-2 $\text{R}^{\text{c}1}$ and consisting of: carbon atoms and 0-2 heteroatoms selected from N, O, and $\text{S}(\text{O})_p$;

R^{d} is, independently at each occurrence, C_{1-6} alkyl, OR^{a} , Cl, F, Br, =O, $-\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{C}(\text{O})\text{Ra}^1$, $-\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{S}(\text{O})_2\text{NR}^{\text{a}}\text{Ra}^1$, $-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{Ra}^3$, $-\text{S}(\text{O})_p\text{Ra}^3$, CF_3 , or phenyl;

R^5 is, independently at each occurrence, C_{1-4} alkyl substituted with 0-2 R^{b} , or C_{1-4} alkyl substituted with 0-2 R^{e} ;

r , at each occurrence, is selected from 0, 1, 2, and 3; and

s , at each occurrence, is selected from 0, 1, 2, and 3.

20. (New) A compound according to Claim 19, wherein:

A is $-\text{C}(\text{O})\text{NHOH}$;

Z is phenyl substituted with 1-2 R^{b} , naphthyl substituted with 1-2 R^{b} , or pyridyl substituted with 1-2 R^{b} ;

Z^{a} is phenyl substituted with 1-3 R^{c} , naphthyl substituted with 1-3 R^{c} , or a heterocycle substituted with 1-3 R^{c} and selected from furanyl, tetrahydrofuranyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isoxazolyl, 4,5-dihydro-isoxazolyl, thienyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyrimidinyl, piperazinyl, piperidinyl, pyranyl, pyrazinyl, pyrazolyl, pyridoimidazolyl, pyrrolidinyl, pyrrolyl, indolyl, indolinyl, benzimidazolyl,

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

benzothiazinyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benzisoxazolyl, benzisothiazolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydro-isoquinolinyl, indazolyl, isobenzofuranyl, isoindazolyl, isoindolinyl, isoindolyl, methylenedioxyphenyl, quinazolinyl, 1,1-dioxido-2,3-dihydro-4H-1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2H-1-benzothiopyran-4-yl, 3,4-dihydro-2H-chomen-4-yl, 2H-chomen-4-yl, and pyrazolo[1,5-a]pyridinyl;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, S(O)_p-O, O-S(O)_p, or S(O)_p-S(O)_p group;

R¹ is selected from Q, C₁₋₆ alkylene-Q, -(CR^aR^{al})_rO(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rC(O)NR^aR^{al}, -(CR^aR^{al})_rC(O)NR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)(CR^aR^{al})_s-Q, or -(CR^aR^{al})_rNR^aC(O)O(CR^aR^{al})_s-Q;

Q is, independently at each occurrence, H, a C₃₋₆ carbocycle substituted with 0-3 R^d, or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-3 R^d;

R² is Q¹ or C₁₋₆ alkylene-Q¹;

Q¹ is, independently at each occurrence, H, phenyl substituted with 0-2 R^d, or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-2 R^d;

R³ is Q, C₁₋₄ alkylene-Q, C₂₋₄ alkenylene-Q, C₂₋₄ alkynylene-Q, -(CR^aR^{al})_rNR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)O(CR^aR^{al})_s-Q, -(CR^aR^{al})_rNR^aC(O)NR^a(CR^aR^{al})_s-Q, -(CR^aR^{al})_rS(O)_p(CR^aR^{al})_s-Q, -(CR^aR^{al})_rSO₂NR^a(CR^aR^{al})_s-Q, or -(CR^aR^{al})_rNR^aSO₂(CR^aR^{al})_s-Q;

alternatively, R¹ and R³ combine, along with the carbon atom to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

alternatively, when R¹ and R³ combine to form a carbocyclic or heterocyclic ring, the R² and R⁴ combine to form a double bond;

R⁴ is Q¹ or C₁₋₆ alkylene-Q¹;

alternatively, R³ and R⁴ combine, along with the carbon atom to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R^{4a} is Q, -CH₂-Q, -CH₂O(CH₂)_s-Q, -CH₂NR^a(CH₂)_s-Q, -CH₂C(O)(CH₂)_s-Q, -CH₂C(O)O(CH₂)_s-Q, -CH₂C(O)NR^aR^{a1}, -(CH₂)_rC(O)NR^aOR^a, -CH₂C(O)NR^a(CH₂)_s-Q, -CH₂NR^aC(O)(CH₂)_s-Q, or -CH₂NR^aC(O)O(CH₂)_s-Q;

alternatively, R¹ and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-3 R^d, provided that n is 0;

alternatively, R³ and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R^{a1} is, independently at each occurrence, H, C₁₋₆ alkyl, phenyl, or benzyl;

R^{a3} is, independently at each occurrence, H, C₁₋₆ alkyl, phenyl, or benzyl;

R^c is, independently at each occurrence, H, OR^a, Cl, F, Br, =O, CF₃, CH₂F, CHF₂, -(CR^aR^{a1})_rNR^aR^{a1}, -(CR^aR^{a1})_rC(O)R^{a1}, -(CR^aR^{a1})_rC(O)OR^{a1}, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rNR^aC(O)R^{a1}, -(CR^aR^{a1})_rS(O)_pR^{a3}, -(CR^aR^{a1})_rSO₂NR^aR^{a1},

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

$-(CR^aR^{a1})_rNR^aSO_2R^{a3}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl substituted with 0-2 R^{c1} , or 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and $S(O)_p$, and substituted with 0-2 R^{c1} ; and

alternatively, when two R^c groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-6 membered carbocyclic or heterocyclic ring D substituted with 0-2 R^{c1} and consisting of: carbon atoms and 0-2 heteroatoms selected from N, O, and $S(O)_p$.

21. (New) A compound according to Claim 20, wherein:

U is absent or is O, NR^{a1} , $C(O)$, $CR^a(OH)$, $C(O)NR^{a1}$, or $NR^{a1}C(O)$;

X is absent or is methylene or butynylene;

Y is absent or is O;

Z is phenyl substituted with 1-2 R^b ;

Z^a is naphthyl substituted with 1-3 R^c , or a heterocycle substituted with 1-3 R^c and selected from furanyl, tetrahydrofuranyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isoxazolyl, 4,5-dihydro-isoxazolyl, thienyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyrimidinyl, pyranal, pyrazinyl, pyrazolyl, pyridoimidazolyl, pyrrolidinyl, pyrrolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydro-isoquinolinyl, imidazolyl, benzimidazolyl, benzothiazinyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benzisoxazolyl, benzisothiazolyl, indolyl, indolinyl, indazolyl, isobenzofuranyl, isoindazolyl, isoindolinyl, isoindolyl, quinazolinyl, 1,1-dioxido-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2*H*-1-benzothiopyran-4-yl, 3,4-dihydro-2*H*-chomen-4-yl, 2*H*-chomen-4-yl, and pyrazolo[1,5-*a*]pyridinyl;

provided that U, Y, Z, and Z^a do not combine to form a N-N, N-O, O-N, O-O, $S(O)_p$ -O, O- $S(O)_p$, or $S(O)_p$ - $S(O)_p$ group;

R^1 is Q, C_{1-6} alkylene-Q, $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q$, or $-(CR^aR^{a1})_rNR^aC(O)O(CR^aR^{a1})_s-Q$;

DOCKET NO.: PH 7287 NP
USSN: 10/697,545

Q is, independently at each occurrence, H, a C₃₋₆ carbocycle substituted with 0-3 R^d, or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from N, O, and S(O)_p, and substituted with 0-3 R^d;

R² is H or C₁₋₆ alkylene-Q¹;

R³ is Q, C₁₋₄ alkylene-Q, C₂₋₄ alkenylene-Q, C₂₋₄ alkynylene-Q, -(CH₂)_rNR^a(CH₂)_s-Q, -(CH₂)_rNR^aC(O)(CH₂)_s-Q, -(CH₂)_rNR^aC(O)O(CR^aR^{a1})_s-Q, -(CH₂)_rNR^aC(O)NR^a(CH₂)_s-Q, -(CH₂)_rS(O)_p(CH₂)_s-Q, or -(CH₂)_rNR^aSO₂(CH₂)_s-Q;

R⁴ is H or C₁₋₆ alkylene-Q¹;

alternatively, R³ and R⁴ combine, along with the carbon atom to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R^{4a} is Q, -CH₂-Q, -CH₂O-Q, -CH₂NR^a-Q, -CH₂C(O)_s-Q, -CH₂C(O)O-Q, -CH₂C(O)NR^aR^{a1}, -C(O)NR^aOR^a, -CH₂C(O)NR^a-Q, or -CH₂NR^aC(O)O-Q;

alternatively, R¹ and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-3 R^d, provided that n is 0;

alternatively, R³ and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

R^a is, independently at each occurrence, H, or C₁₋₄ alkyl;

R^{a1} is, independently at each occurrence, H, or C₁₋₄ alkyl;

R^{a3} is, independently at each occurrence, H, C₁₋₄ alkyl, phenyl, or benzyl;

R^c is, independently at each occurrence, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, OR^a , Cl, F, Br, =O, CF_3 , CH_2F , CHF_2 , $-NR^aR^{a1}$, $-(CR^aR^{a1})_rC(O)R^{a1}$, $-(CR^aR^{a1})_rC(O)OR^{a1}$, $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$, $-(CR^aR^{a1})_rNR^aC(O)R^{a1}$, $-(CR^aR^{a1})_rS(O)_pR^{a3}$, $-(CR^aR^{a1})_rSO_2NR^aR^{a1}$, $-(CR^aR^{a1})_rNR^aSO_2R^{a3}$, or phenyl; and

alternatively, when two R^c groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-6 membered carbocyclic or heterocyclic ring D substituted with 0-1 R^{c1} and consisting of: carbon atoms and 0-2 heteroatoms selected from N, O, and $S(O)_p$.

22. (New) A compound according to Claim 21, wherein:

U is absent or is O, NR^{a1} , $C(O)$, or $CR^a(OH)$;

Y is absent;

R^1 is H, C_{1-4} alkylene-Q, $-(CH_2)_rNR^a(CH_2)_s-Q$, or $-(CH_2)_rNR^aC(O)O(CR^aR^{a1})_s-Q$;

R^2 is H, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, or $CH(CH_3)_2$;

R^3 is Q, C_{1-4} alkylene-Q, $-(CH_2)_rNR^a(CH_2)_s-Q$, $-(CH_2)_rNR^aC(O)(CH_2)_s-Q$, $-(CH_2)_rNR^aC(O)O(CR^aR^{a1})_s-Q$, $-(CH_2)_rNR^aC(O)NR^a(CH_2)_s-Q$, $-(CH_2)_rS(CH_2)_s-Q$, or $-(CH_2)_rNR^aSO_2(CH_2)_s-Q$;

R^4 is H, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, or $CH(CH_3)_2$;

alternatively, R^3 and R^4 combine, along with the carbon atom to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ and substituted with 0-2 R^d ;

R^{4a} is Q, $-CH_2-Q$, $-CH_2O-Q$, $-CH_2NR^a-Q$, $-CH_2C(O)_s-Q$, $-CH_2C(O)O-Q$, $-CH_2C(O)NR^aR^{a1}$, $-C(O)NR^aOR^a$, or $-CH_2C(O)NR^a-Q$;

alternatively, R^1 and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of:

carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-3 R^d, provided that n is 0;

alternatively, R³ and R^{4a} in Formula I combine, along with the carbon atoms to which they are attached, to form a 5-6 membered carbocyclic or heterocyclic ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^d;

r, at each occurrence, is selected from 0, 1, and 2; and

s, at each occurrence, is selected from 0, 1, and 2.

23. (New) A compound according to Claim 22, wherein:

U is O, NR^{a1}, or CR^a(OH);

Z^a is naphthyl substituted with 1-3 R^c, or a heterocycle substituted with 1-3 R^c and selected from pyridyl, quinoliny, imidazolyl, benzimidazolyl, indolyl, 1,1-dioxido-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2*H*-1-benzothiopyran-4-yl, 3,4-dihydro-2*H*-chomen-4-yl, 2*H*-chomen-4-yl, pyrazolyl, and pyrazolo[1,5-*a*]pyridinyl;

R^b is, independently at each occurrence, H, C₁₋₆ alkyl, OR^a, Cl, F, Br, -NR^aR^{a1}, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^{a1}, -S(O)₂NR^aR^{a1}, -NR^aS(O)₂R^{a3}, -S(O)_pR^{a3}, or CF₃;

R^c is, independently at each occurrence, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, OR^a, Cl, F, Br, =O, CF₃, -NR^aR^{a1}, -(CR^aR^{a1})_rC(O)R^{a1}, -(CR^aR^{a1})_rC(O)OR^{a1}, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rNR^aC(O)R^{a1}, -(CR^aR^{a1})_rS(O)_pR^{a3}, -(CR^aR^{a1})_rSO₂NR^aR^{a1}, or -(CR^aR^{a1})_rNR^aSO₂R^{a3}; and

alternatively, when two R^c groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-6 membered saturated ring consisting of: carbon atoms and 0-1 heteroatoms selected from N, O, and S(O)_p.